BULLETIN

of the

ONTARIO COLLEGE OF PHARMACY

Vol. VI, No. 3 TORONTO, Ontario May, 1957

H. J. Fuller, Editor

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The Ontario College of Pharmacy is the pharmaceutical licensing body for the Province of Ontario, Canada. All pharmacists licensed in Ontario are *IPSO FACTO* members of the College.

The majority of contributors to the Bulletin are members of the Faculty of Pharmacy, University of Toronto. However, contributions are welcomed from all members of the College.

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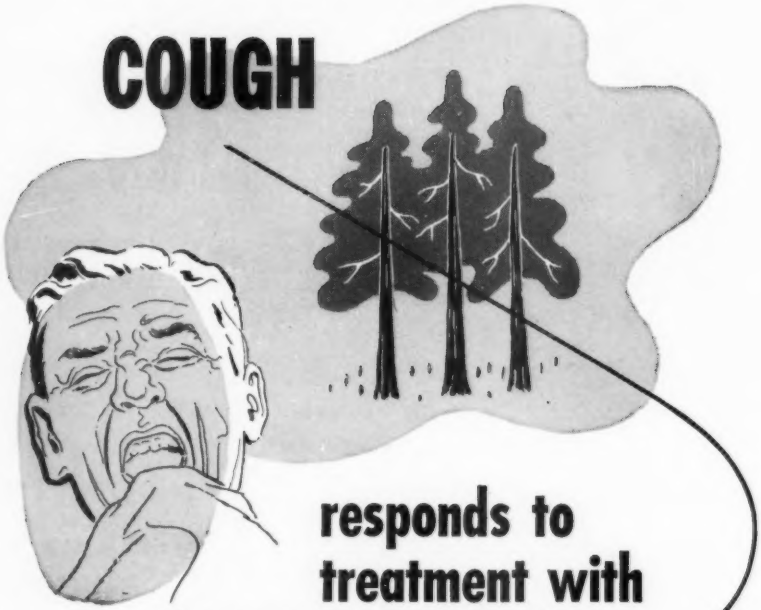

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PROFESSIONAL FEES

In the March issue of the Bulletin I attempted to set forth some ideas concerning prescription pricing and cost accounting. After reviewing some methods of costing I suggested that "if you conceive pharmacy to be a profession and the compounding and/or dispensing of a prescription a personnal service to a patient, your knowledge of YOUR costs is still essential but only as a management tool and as a measure of productive efficiency. Costs are only one element in the determination of the price of a prescription. The professional fee is of equal importance." Put in a slightly different way, one may say that all costs must be recovered if one is to remain a "going concern" in any kind of activity in life. The doctor, the dentist, the lawyer must recover his costs from his fees but his fees are not based on costs. The theory of value that goods and services have value because they cost so much to produce was discarded by economists some decades ago.

The Basis of Value

By value, the economist means how much of one good or service one must give to obtain a certain amount of another good or service. It is exchange value that is meant and when expressed in terms of money it is called price. All economic values rest, not upon labour or cost but upon **utility** and **scarcity.** They arise not because of anything inherent in a good, but as a result of human judgment. The source of value is to be found in men and not in things. Goods and services have value only in proportion to the satisfactions which they yield. This ability of goods and services to satisfy human wants is called **utility.** We have all heard something of the so-called Law of Supply and Demand of the classical economists which assumes that price is determined by the relationship of supply to demand at a given time and a given place. Utility is on the side of demand and is coupled with purchasing power or the ability to pay.

The other element of exchange value is **scarcity.** It is on the side of supply. Anything that is not free is scarce. However, it is a relative term. Some things are relatively plentiful and therefore not very scarce. Others are scarce indeed. Scarcity is also an individual term and also a social term. Wheat may be scarce to the unemployed individual who does not have any money while at the same time it may be plentiful to the nation. The Dominion Bureau of Statistics reports that on March 31, 1957 Canada held a record 831,306,000 bushels of wheat, including a peak of 459,000,000 on farms. The overall wheat holdings were 80,000,000 bushels higher than a year ago and up about 49,000,000 bushels from the previous record of 762,400,000 in 1943.

On April 23, the **Globe and Mail** reported that "Famine menaces 1,000,000 persons in Eastern India. Floods, hail and thunderstorms destroyed much of Bihar State's food crop. Bihar needs 400,000 tons of food grains to tide the population over until new crops come in." Grain in India is scarce. Not only that, so is purchasing power. The per capita income in India is only about one sixteenth of what it is in Canada. If India possessed the purchasing power to buy Canadian wheat then India would be potiential demand for Canadian wheat. In a free market, the exchange value or price would be the relationship of this potential demand to supply. In a free market, exchange value or price to the individual customer depends on utility (coupled with ability to pay) and scarcity. No individual customer nor any individual farmer would have the ability to influence price appreciably.

In Canada, there is a sort of floor under the price of wheat. The Federal government now has support programs for butter, eggs, hogs, fowl, and skimmed milk. If the market price of any of these items falls below certain set minimums, the government steps in and buys the surplus thus pulling the price back to at least the floor by influencing demand. These agricultural prices support programs have resulted in net losses of $79,500,000 to the federal government during the past five years. The floor prices are intended to help **keep up** the farmer's income. We must conclude then, that **all the market does for these items is to give effect to the institutional patterns and arrangements which prevail in the structure of society itself.**

Prescripitons

If we now turn to prescriptions, the value of a prescription is its utility to the patient. The pharmacist will exchange the prescription for his costs plus whatever he desires to maintain his standard of living in the community, just as the farmer has his notion of his standard of living. The value or price of the prescription will be the relationship between the utility to the patient and the supply, that is, the number of pharmacists willing to provide the prescription service. The cost has little to do with the matter. In the last analysis, bare cost would be just sufficient to keep the pharmacist alive if predatory competition were allowed to reign. The pharmacist, no more than the farmer, is unwilling to produce just to stay alive. The standard of living of the community has had its impact on him and he desires a share in the prosperity of the country as a whole. The difference between the farmer and the pharmacist is that the farmer has the government on his side attempting to get higher than market prices for what he produces. The pharmacist has to persuade the community that his services are as vital to the health and welfare of the community as horse racing or whiskey on which the community spends as much as it does for prescribed medicines.

Professional Services

When the pharmacist dispenses a prescription he does not just **sell** a bottle of medicine in the market place. A prescription is not "trade goods," an article of ordinary commerce, capable of being bought and sold by anyone. A prescription is only for the use of one person and that person cannot sell it as an article of trade. There is no common element in prescriptions. The services rendered by the pharmacist in dispensing and/or compounding a prescription are of a professional nature, requiring specialized knowledge and judgment and the reward he gets for such services is therefore a **fee.** The knowledge the pharmacist possesses to place in the hands of the patient exactly what the doctor orders is a **professional service** to the patient. The **fee** is in part compensation for the long and arduous years of studying and training necessary to equip the pharmacist with this knowledge.

In Canada and the United States, pharmacists have been all too prone to consider prescriptions as mere merchandise. For years the price of a prescription has been calculated as so much markup on the cost of the ingredients and container as if professional services were a function of the cost of the ingredients. In recent years there have been various schemes of adding a dispensing or professional fee to the cost of ingredients and container plus markup. This professional fee is applied in an eratic and arbitrary fashion. For example, the National Association of Retail Druggists (U.S.) Suggested

Prescription Pricing Schedule suggests 60 cents as a professional fee for capsules, pills or tablets up to 50 and seventy cents if the prescription calls for 75 capsules, pills or tablets. No such functional relationship exists. The same professional service is performed whether the prescription calls for 50 or 75 pills, capsules or tablets. While calling it a professional fee, this method still treats prescriptions as merchandise. My own "Method of Estimating Professional Dispensing Fees" circulated freely in Ontario must be charged with this error. Further, the amount of this professional fee has been trifling, usually 25, 35 or 50 cents like handing the shoe shine boy a tip or leaving a tip for the waitress in a restaurant.

A New Philosophy

Debating this whole subject in the senior class recently, one student came up with an entirely new approach. Why not turn the scheme around the other way, that is, make a definite standard charge of say $2.00 as a professional fee for dispensing or compounding a prescription regardless of the cost of ingredients or the time spent in dispensing or compounding. Then add the wholesale cost of the ingredients and container. The pharmacist would then have to arrange his affairs to pay all his overhead out of his professional fees just as the doctor pays his office expenses, the salary of his nurse or secretary, and the cost of operating his car. This fee could be common or standard for a community by mutual agreement. Most doctors in the same community charge the same fee for an office call. One may attend twice as many patients as another. One may drive a Cadillac and another an Austin. One may employ a nurse to answer the phone and act as his secretary, another may permit his wife to perform these functions but their fees are the same.

Medical associations compile schedules of fees and are not charged by government for price fixing because their fees are for services. They are not fixing the price of an article in trade. Likewise if pharmaceutical associations compiled schedules of fees and gave the medicines at cost, government could not charge them with price fixing since the government could hardly demand that medicines be given away or sold below cost.

Conclusions

I realize that this is a tremendous innovation and likely to stir a great deal of comment one way and another. However, to me two things stand out very clearly in this era of the changing practice of pharmacy.

First: A great many people, both in and out of the health professions, are predicting that sometime in the forseeable future we will have a comprehensive health insurance scheme that will include medicines. If this happens, where do we stand? If we consider prescriptions as merchandise, the demand side of the supply and demand relationship will change. Instead of millions of potential customers on the demand side, we will have one big customer, the government. When there is only one seller, the economist calls the market situation **monopoly** and this term has varied significance for most people. When there is only one buyer, the economist calls the market situation **monopsony.** It is not a pretty word, but it means the same as monopoly does when there is only one seller. Under monopsony pressure on the seller can be as inconsiderate as pressure on the customer when there is monopoly. Further, when we advertise "When you need a

prescription depend on your pharmacist—Your pharmacist—the only merchant in your community who must have a university degree . . . " what can we expect government to say? Government will say, "You are **mere** merchants. You sell prescriptions. This is what they cost you. This is what we will pay you." And you won't like it a bit.

In England, the initial rate paid the pharmacist under the National Health Service when it was established in 1948, was 33% on cost of ingredients. This is only 25% on selling price. In 1950 the rate was reduced to 25% on cost or a mere 20% on selling price. Also in 1950 the pharmacist was permitted to obtain a one shilling professional fee from the patient but this must be deducted from the bill the pharmacist sends the government, namely 25% on cost. This ritual of collecting a shilling as a professional fee in no way compensates the pharmacist for his professional services. The rates still remain 25% on cost of ingredients. This reduces the pharmacist to the status of a mere tradesman with only one customer, the government.

If we advertise ourselves to government and the public as merchants with a university degree, how can we expect either to be willing to pay us for professional services through professional fees? Such advertising is building the wrong institutional patterns and arrangements in the structure of society and if persisted in and not corrected will reduce the pharmacist to the function of a domestic servant in the national household when and if a comprehensive health insurance scheme including medicines arrives. Equality of opportunities to share in the prosperity of the national economy will be an empty phrase for the pharmacist.

Second. The era of gadgeteering in prescription pricing should be discontinued. The pharmacy student must study botany, zoology, physics and related subjects as a foundation for later study of organic chemistry, pharmaceutical chemistry, physiology, pharmacology, and dispensing. The student also studies economics, accounting, marketing, and management. These are all difficult subjects. But after the student has been graduated a few years something seems to happen to him. When faced with the problem of setting up some standard rational basis of pricing prescriptions, he says, "Oh! I could never do that. Give me a gadget, a chart, a wheel, a card or something that will figure it out for me." This attitude is the antithesis of all that we have been trying to say and teach.

H. J. FULLER.

THE SECOND HOSPITAL PHARMACY SURVEY

Health insurance plans and the costs of hospital care are issues which have challenged the interest of all Canadians during the past year. In Ontario, much publicity has been given to the proposals of the Provincial Government through the press, radio and television. Pharmacists are viewing these measures with some concern because of their impact on both their professional services and private lives.

In countries such as Great Britain and Australia, where National Health Insurance schemes are presently in operation, much controversy has arisen over the handling and pricing of drugs and pharmaceuticals. The lack of uniform pricing schedules and insufficient statistical data, pertaining to hospital pharmacy has confused the

issues. At times, disagreements within the various groups in the profession, have placed the pharmacist in an unfortunate bargaining position.

January, 1959, the date proposed for the implementation of Hospital Care Insurance for Ontario, leaves little time for reflection, if we are to profit by the experience of some of our colleagues in other parts of the world. An intelligent and factual appraisal of existing conditions and administrative procedures will enable us to plan wisely for future commitments.

The First Survey on Hospital Pharmacy, conducted by the Faculty of Pharmacy, University of Toronto, last year, indicated that of the 673 hospitals approached, only 199, or 29.5 per cent employ a pharmacist. In Ontario, only 26.5 per cent reported that one or more pharmacists were members of the hospital staff. At present, neither the Pharmacy Act nor the several Provincial Acts which govern hospitals in this Province make provision for pharmaceutical service in hospitals. Under these circumstances, who will speak for Pharmacy when the handling and pricing of drugs and pharmaceuticals are questioned?

Personnel distribution in Canadian hospitals employing a pharmacist and a comparison of present staffing patterns with recommended staffing patterns, based on bed capacity, were also reported in the Survey. In hospitals of 400 beds or more, Canadian hospitals fell far below this standard. With the present shortage of pharmacist personnel, how are future requirements to be met? The introduction of Health Insurance schemes in other countries has resulted in an increase in the use of hospital facilities. The shortage of pharmacists, it is reasonable to suppose, will become more acute in the future.

Hospital Pharmacy in Canada is growing. The Canadian Society of Hospital Pharmacists celebrates its tenth anniversary this year. The broadening of the Canadian Pharmaceutical Association to include hospital pharmacists and members of the Canadian Conference of Pharmaceutical Faculties has enabled these groups to work more closely with the other branches of the pharmaceutical profession. The advent of Health Insurance will present an excellent opportunity for further united effort.

With these facts in mind, the Faculty of Pharmacy, University of Toronto has conducted a Second Survey in Hospital Pharmacy Practice. This project has been designed to obtain more specific information on some of the economic aspects of Hospital Pharmacy Administration, regarding prescription pricing and charges for drugs and pharmaceuticals. To date the total number of replies received has been most gratifying.

We believe that this information, together with the data established through the Canadian Pharmaceutical Association Annual Survey during the past fifteen years, will be a most useful tool in planning a course of action in the future. However, this is only a segment of the total picture. Provincial legislation, which will encompass hospital pharmacists and pharmcies in hospitals, is necessary before the organization and administration of all pharmaceutical services can be outlined in a Health or Hospital Insurance program. Complete and comprehensive results will produce statistical data which will benefit all pharmacists. Have you returned that questionnaire? Your co-operation will be greatly appreciated.

I. E. STAUFFER.

OPHTHALMIC SOLUTIONS

Ophthalmic solutions have given rise to countless problems since their introduction into pharmacy and medicine. The problems have been primarily those of preservation, stability and chemical compatibility.

The hospitals have been particularly concerned because of the large number dispensed and the use of stock solutions, but more recently it has been brought home forcibly to the retail profession.

The majority of substances dispensed are alkaloids or materials generally susceptible (that is providing a media) to mold or bacterial growth. In the pharmacy, as many of us will admit, often little care is taken as far as sterility is concerned, and even as far as buffering or pH is concerned. The eye is a very delicate tissue. It is difficult to get a new one or to get the old one repaired.

Looking at Some Facts

There are many organisms that can cause infection but the real offender is Pseudomonas aeruginosa (B. pyocyaneus). It can cause the formation of corneal ulcers. It is dangerous.

In one report only, 5 clinical cases of 18 were caused by Pseudomonas aeruginosa from contaminated eye drops. This prompted one university to have eye prescriptions made up by two of the better pharmacies, by a hospital, and at the university under controlled conditions.

The No. 1 pharmacy prepared atropine and pilocarpine solutions —2 strengths of each — all were heavily contaminated.

The No. 2 pharmacy prepared certain prescriptions — all were so heavily contaminated the culture tubes were thick.

The hospital used a preservative — no contamination was found even though they filtered through paper.

The pharmacies prepared the solutions the way they ordinarily did it and it simply illustrates the point of contamination. Many other cases could be cited.

Eye specialists have intimated that they don't know whether to send their patients to the pharmacy or not. From different outlets the prescriptions varied as regards, clarity, stability and therapeutic activity; this was particularly noted in connection with methyl cellulose but pseudomonas was cited as damaging and there is quite a bit of it about. It is a problem that should interest us all.

From a recent survey it would appear in general that ophthalmologists are not in complete agreement as to the buffering, preservation, and isotonicity of ophthalmic solutions but the majority of them reported that they wanted to be detailed on special services the pharmacist could offer them in compounding their prescriptions.

It is more serious in industry because of the time lag between the making of a batch of eye material and the sale. Extemporaneously, of course, this does not exist and a normal period of use might be two weeks.

However, the United States Food and Drug Administration did something about it. They made regulations saying that if the solution was not sterilized then it might be regarded as adulterated. The solutions should:

1. Contain one or more suitable harmless substances to prevent growths **or**
2. Be packaged as to volume and type of container and so labelled as to the duration of use with warnings.

This is good legislation.

In the average retail pharmacy it is really impossible to prepare sterile eye solutions without proper equipment or techniques.

Important Factors in Preparing Ophthalmic Solutions

1. **Clarity of the Solutions**

The solutions must be free of all contaminating particles, that is, dust, dirt, lint, etc. which might produce irritation and in addition a non-elegant preparation.

This of course means that the solutions must be filtered. Filtration may be simply performed by means of filter paper or by means of more useful devices, the sintered glass filter, or filtering candles made of diatomaceous earth, clay, silica or pyrex glass. These special types of apparatus are most useful if properly selected since they will not only remove insoluble material but bacteria as well. However, they require a suction pump for operation.

2. **Elimination or Control of Micro-organisms**

As indicated previously this is of common occurrence and can be serious. The solution should be free of micro-organisms or their growth arrested when prepared in the dispensary and sufficient care taken in so doing that they remain uncontaminated when used by the patient.

Nothing we use in preparing ophthalmic solutions is in a sterile condition. Prescription dropper bottles are made using great heat and generally are packaged in a short time. Contamination here, it is felt by some authors, would not be of major concern but it should always be remembered that the pharmacist may have the bottles lying around in the dispensary for some time and often unstoppered.

The chemicals used in preparing ophthalmic medications are not sterile but are not major sources of contamination.

The equipment we use is definitely not sterile but if washed and rinsed thoroughly it again is not a major source of contamination.

Distilled water is one of the serious offenders. It is not necessary here to go into great detail, but many of us will agree that the bottle may stand around for long periods of time, be opened and closed on many occasions, and when we prepare the ophthalmic solution we simply pour the water in and dispense. Obviously, it may be heavily contaminated. If it is a fresh bottle, or there is a special closure and delivery device, contamination is greatly reduced.

The active ingredients in eye solutions are often alkaloids or substances which micro-organisms use as a growth substrate, that is, as food for growth. The keeping of stock solutions of alkaloids and certain other materials can therefore be a source of contamination unless sterilized or preserved. Very frequently, distilled water of the dispensary with no treatment is used to prepare the alkaloidal solution and after standing for a week or two, growth is often observed.

3. **Hydrogen Ion Concentration**

The pH of an ophthalmic solution is of great importance since irritation might occur if the solution is not near the pH of the lacrimal secretion. In addition, many substances used in eye solutions must have certain pH conditions for maximum stability. A low pH, that is, on the acid side of neutrality (between 1 and 7) is desirable for most ophthalmic materials since bacterial growth is inhibited. On the other hand, if too acid, the eye is irritated. The chemical preservative used (and which we shall mention presently) may not be so active at low pH. It can be seen then that a compromise must often

be made between the optimum conditions necessary for stability and therapeutic activity.

The pH of the lacrimal fluid (tear secretion) has been reported by many investigators and varies from 6.3 to 8.6. The most common value used is about 7.2 to 7.4. The adjustment of the pH is brought about by means of buffer solutions, that is solutions that can be used for maintaining a definite pH value within narrow limits.

4. **Isotonicity**

It is an old and well-known fact to pharmacists that a solution in contact with body fluids should have the same osmotic concentration as the body fluid with which it is in contact. They are then much less likely to produce irritation. The eye can tolerate without apparent irritation or discomfort solutions having a wide range of isotonicity providing the pH is controlled.

It has been reported that the addition of non-medicament solutes to make ordinary eye drops isotonic is unnecessary and increases the danger of the pharmacist making an error, that is, as far as ordinary drops are concerned. From this statement it would appear that isotonicity is of no real concern, but it should always be remembered that adjustment may be worth while since a bite or nip in the eye is often experienced in a solution that is not isotonic.

5. **Preservatives**

The use and choice of a preservative is of the greatest importance in the preparation of eye solutions. The addition of a preservative to solutions that are not prepared under sterile conditions can never serve as a substitute for sterile preparations. However, the use of a preservative is absolutely necessary, whether the solution is already sterile or not. If the physician does not want the preservative that is a different matter. There is no single agent for the self-sterilization of eye solutions at the present moment because of incompatibilities and none are absolutely reliable under all conditions.

Preservatives are not used to sterilize solutions for the eye without recourse to other methods such as heat and filtration, but they do prevent the growth of micro-organisms, particularly when the patient is continually opening and closing the bottle with accompanying contamination.

The Requirements of a Good Preservative

1. Non-toxic (harmless but strong enough).
2. Non-irritating.
3. Must remain active indefinitely.
4. Non-allergenic or sensitizing.
5. Compatible with most of the drugs and excipients used.
6. Must not interfere with the therapeutic activity or chemical stability.

There are cases where the medicament itself may be enough to prevent growth but they are infrequent.

One thing must be remembered: **the preservative is absolutely necessary.** Filters will not do the job if the bottle is not sterile, nor will a sterile solution remain so once opened.

Chlorbutol (Chlobutanol)

This is a very useful preservative but volatile and of limited solubility. It should be finely divided and triturated thoroughly with some of the diluent, then transferred to a bottle where it can be shaken

frequently until completely dissolved. It is deactivated by alkaline solutions and by autoclaving.

Esters of para Hydroxy Benzoic Acid

The methyl and propyl esters of para hydroxybenzoic acid appear together in Preserved Water of the Canadian Formulary which is as follows:

Methyl parahydroxybenzoate	0.025%
Propyl parahydroxybenzoate	0.015%

They are of limited solubility and are preferably dissolved with the aid of heat.

Benzalkonium Chloride

A quaternary ammonium surface-active agent widely used in preserving eye solutions. It lowers surface tension and has been suggested as increasing penetration into eye tissue while maintaining a more persistent therapeutic effect. Many concentrations ranging from 1 : 5,000 to 1 : 50,000 have been employed.

Phenylmercuric Nitrate

This mercury compound has been widely used in concentrations of 1 : 25,000 to 1 : 100,000. The solubility of phenylmercuric compounds is low and a little heat may be used.

The four mentioned above have been used most widely but there are others:

Phenol; Thimerosal; Phemerol Hydrochloride; Benzethonium Chloride (Hyamine 1622); Benzyl alcohol; and Phenylethyl alcohol.

Procedures in Preparing Ophthalmic Solutions

It must be realized that whereas autoclaving is desirable for sterile preparations it cannot be used for all eye solutions since some of the materials are sensitive to heat. Filtration and the use of preservatives are the methods of choice.

It is difficult to lay down exact procedures for the practising pharmacist since there are so many ways of doing things; and provided certain principles are maintained, there is usually no problem. It is perhaps useful to mention the important principles in the preparation of ophthalmic solutions.

Sterile, distilled water should be used. The final containers, droppers, etc. and the utensils used in the operation should be sterilized. The solution containing the preservative should be prepared under as aseptic conditions as possible and filtered into the sterile container.

Using the proper preservative, which will be indicated later in the formulas presented, this procedure gives solutions which although not sterile are satisfactory from the dispensing point of view.

Formulations

The principles behind the proper compounding and dispensing of eye solutions have been discussed in a general way, and while by no means complete, will have suggested, along with the apparatus, a plan of attack around which the pharmacist may develop his own procedures.

It is very useful to know the better formulations available and in particular the preservatives and buffers that may be used. Many reports have appeared in the literature concerning the effect and compatibility of various preservatives and buffer systems. It is impossible to survey them all, but a few of the more generally useful have

already been presented and the following formulas and preservatives.

Comments are presented from various text-books and from the literature in the hope that they may provide a ready reference for compounding of such solutions, and provide a basis for future ophthalmic considerations by the pharmacist. Ophthalmic ointments, creams, etc., have not been touched upon in this paper, since it was felt that more time would be required in order to do a thorough treatment of the subject.

Solution for Eye-Drops—B.P.C., 1954.

Liquor pro Guttis.
Methyl Hydroxybenzoate (Methyl Paraben) .....0.22g. (1 gr.)
Propyl Hydroxybenzoate (Propyl Paraben) .....0.114g. (½ gr.)
Distilled Water, freshly boiled and cooled to 1000.00 ml. (10 fl. oz.
Dissolve with aseptic precautions.

The above solution is very similar in composition to Preserved Water of the C.F. 1949 which was presented in an earlier part of this paper. The C.F. preparation is a little stronger.

The following Eye-Drops are formulated in the B.P.C. with a vehicle or base of the above Solution for Eye-Drops: Amethocaine 1%; Atropine Methonitrate 1%; Atropine Sulphate 1%; Carbachol 0.8%; Cocaine 2%; Cocaine and Homatropine 1%; Copper Sulphate 0.5%; Ethylmorphine 1%; Fluorescein 2%; Homatropine 2%; Hyoscine 0.25%; Lachesine 1%; Penicillin; Physostigmine 0.5%; Pilocarpine 1%; Silver Nitrate 0.5%; Sulphacetamide Strong 30%; Sulphacetamide Weak 10%.

BUFFER SOLUTIONS

Borate Buffer at a pH of about 5

Boric Acid 2%
Phenylmercuric nitrate 1:25,000
Distilled Water q.s. .....

The final solution contains the preservative phenylmercuric nitrate in a concentration of 1 in 25,000. This buffer is useful for preparing eye drops containing Cocaine, Dionin, Metycaine, Nupercaine, Optochin, Phenacaine, Pontocaine, Procaine, Syntropan, Zinc, Physostigmine, Tetracaine, Dibucaine, Piperocaine, Prostigmine.

Phosphate Buffer at about pH5

Sodium Acid Phosphate ..... 4 g.
Disodium Phosphate (anhydrous) ..... 4.73 g.
Sodium Chloride ..... 4.3 g.
Benzalkonium Chloride 1:10000
Distilled Water q.s. ..... 1000 ml.

This solution is useful in the preparation of eye drops containing Atropine, Pilocarpine, Ephedrine, Eucatropine, Homatropine, Phenylephrine, Scopolamine.

Vehicle for the Sulpha Drugs

Sulphonamide (as the Sodium salt) ..... q.s.
Phenylmercuric Nitrate 1:25,000
Sodium Sulphite anhydrous 0.1%
Distilled Water ..... q.s.

This solution is useful in the preparation of eye drops containing the Sodium salts of the Sulphonamide drugs such as the following: Sodium Sulphadiazine, Sodium Sulphacetamide, Sodium Sulphathiazole, Sulphisoxazole Diethanolamine.

Some Specific Formulations

Eye-Drops of Fluorescein Sodium

Sodium Fluorescein	q.s.
Phenylmercuric Nitrate	1:25,000
Distilled Water	q.s.

Eye-Drops of Eserine Salicylate

Physostigmine Salicylate	0.5 g.
Sodium Sulphite	0.1 g.
Phenylmercuric Nitrate	1:100,000
Boric Acid	22.0 g.
Distilled Water q.s.	1000.0 ml.

Table—Effects of Chemical Preservatives Observed in Ophthalmic Solutions

Medicinal Agent Added to Solution of Preservative	% Concn.	Preservative in Aqueous Vehicle: Phenol 0.5%	Chlorobutanol 0.5%	Benzalkonium Chloride 1:5000	Thimerosal 1:20,000	Me. Paraben 0.18% Pr. Paraben 0.02%	Distilled Water
Atropine Sulphate	1.0	sl. P	sl. P	sl. P	sl. P	sl. P	sl. P
Dextrose	5.6			sl. P			clear
Mercuric Chloride	1.0	P		T	P	P	clear
Mercury Succinimide	1.0				P		
Phenobarbital Sodium	1.0		P(c)			P (c)	clear
Physostigmine Salicylate	0.5	(r)	(r)	T (r)	(r)	(r)	sl. P
Pilocarpine Hydrochloride	1.0						
Potassium Iodide	1.4			sl. T			
Silver Nitrate	1.0	sl. P	sl. T	P(b)S(y)	P (y)		clear
Sodium Borate	1.0			T			clear
Sodium Nitrate	1.5			P (c)			clear
Sodium Sulfadiazine	5.0	P S(y)	P	P	P (c)	P	clear
Sodium Sulfathiazole	5.0	P(c)S(y)	P(c)	P (b)	sl. P	P	clear

ap—precipitate, S—solution, T—turbidity, (b)—brown, (c)—crystalline, (r)—rose, (y)—yellow, sl.—slight.

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Methyl Cellulose in Ophthalmology

Methyl Cellulose has been widely used in eye solutions for the past few years, and with great success. It was considered in earlier days as a medium for contact lenses since it has about the same refractive index as the cornea and helped position the lens and maintain in place. It is a thickening agent and aids in the suspension, if necessary, of active ingredients. It is non-irritating and chemically inert, and can be sterilized by boiling. Solutions of the cellulose do not support bacterial or mold growth.

Methyl Cellulose dispersions help retain medicinal substances in closer contact with the eye. Drops may be held in the conjunctival sac even with blinking. If blinking takes place the drops are caught on the eye lashes and on opening the eye they flow back into the sac. Occasionally an unsightly white precipitate forms on the lashes but can be washed off with a wet pad or cloth. There have been many thousands of clinical cases with rarely an objection.

Artificial tears have been sold which are simply methyl cellulose in water, buffered or with saline.

The pharmacist must recognize certain important features in the use of methyl cellulose. The solutions must be properly prepared using cold or ice water and stored in a refrigerator at about 10°C. The grade of methyl cellulose purchased must be pharmaceutical, not technical. Dispersions cannot be filtered but can be permitted to stand when the impurities will settle out. The supernatant is then decanted. Alternatively a centrifuge may be used. The solutions must be made with pure distilled water or sterile water as pointed out previously under techniques. Any viscosity may be used but 4,000 c.p.s. is common.

The Pharmacist must record which one he uses, the manner of preparation, and all detail so that he may repeat the preparation accurately. It has been shown recently that methyl cellulose in buffered solutions does not appear to interfere with the buffering actions of certain common buffer systems and concentrations of sodium chloride of 1.4% or less have little effect on the viscosity of a 1% dispersion. The viscosity of methyl cellulose dispersions generally increases as the pH increases.

The majority of the ophthalmic medications used can be dispensed with methyl cellulose and many of the newer drugs such as aureomycin, terramycin, neomycin, chloramphenicol, cortisone, etc. are satisfactory.

Contact Lens Solution

1.

Sodium Borate (10 water)	11.5 g.
Boric Acid	4.9 g.
Sodium Chloride	1.2 g.
Potassium Chloride	0.2 g.
Calcium Chloride (6 water)	0.2 g.
Distilled Water q.s.	1000.0 ml

   The pH of this solution is about 8.7.
2. A solution of Sodium Bicarbonate 1.5% (approx. pH 8.2).

Tear Substitutes

1. Gelatin 0.1% in isotonic solution pH 7.6.
2. Methyl Cellulose (4000 c.p.s.) 0.33% in either isotonic Sodium Chloride solution or equal parts of Sorenson's Phosphate Buffer solution pH 6.8 and isotonic Sodium Chloride solution. The addition of Benzalkonium Chloride 1:50,000 is advisable.

The cleaning of contact lenses is important since dirt and oil secretion accumulates. The lenses may be simply cleaned by using a suitable wetting agent such as Benzethonium Chloride 1:50,000 in a Boric Acid solution of about 2%.

Benzalkonium Chloride may be used for the same purpose. The lenses are left immersed in the solution until ready for use when they are removed, quickly shaken and inserted without rinsing.

EYE LOTIONS

Eye lotions present no special problems. They are generally quite simple solutions which must be freshly prepared, but should not be preserved unless the physician so directs. If preservation is employed, the minimum concentration of preservative should be used since the lotion may be in immediate contact with the eye for a longer period of time and is of larger volume. All the precautions outlined in the preparation of eye drops should be employed for eye lotions.

Eye lotions are a type of preparation that can lead to a spread of infection over a whole eye and/or the other eye by virtue of the very nature of their manner of use, and members of a family using the same eye cup may contact an infection from another since the eye cup is generally not sterilized and an eye solution frequently returned to the same bottle. Just as in the case of the eye dropper where the pharmacist should advise the patient not to place it on a surface or permit contact with other objects, or even with the eye, so here should the pharmacist issue an admonition of care and caution.

APPARATUS

From the practical standpoint, all the pharmacist needs is a clean porcelain vessel, or preferably stainless steel, in which the bottles, droppers, graduates, etc. can be boiled in distilled water before use and a pair of tongs for removing them. Any suitable pyrex glass flask or beaker or stainless steel vessel may be used for boiling the distilled water (sterile ampoule water is most useful).

If a stock preserved solution of any kind is kept, it should be prepared with boiled distilled water (or sterile water from ampoules or purchased in larger volumes) and placed in a sterile bottle, tightly stoppered.

Filtration may be performed through filter paper or a small pledget of cotton in a funnel which has at least been boiled as mentioned previously, in distilled water. If filter paper is used it must be of the finest quality hard paper. Because of the use of non-sterile materials such as cotton or filter paper some authors do suggest not filtering at all.

G. C. WALKER

CHROMATOGRAPHY AND ION EXCHANGE

Part II. Ion Exchange

The importance of chromatography in effecting quantitative separations has been discussed in Part I of this work. Ion exchange is another method for such separations. The two processes are superficially similar in that, in both cases, a glass tube is filled with a column of granular solid through which the liquid sample is allowed to percolate. However, the principles of chromatography and ion exchange are entirely different, the latter applying only to ionized substances.

An ion exchange reaction is essentially a chemical double decomposition:—

$$A^+B^- + C^+D^- = A^+D^- + C^+B^-$$

A useful ion exchange substance should be insoluble and have a capacity to absorb ions of the same charge, reversibly. When these conditions exist, the above equation will, in essence, become:—

$$A^+B^- + D^- = A^+D^- + B^-$$

Macromolecular organic compounds containing numerous acidic or basic groups, and some natural and synthetic aluminosilicates are

utilized for cation and anion exchange. Cation exchangers, therefore, contain numerous negatively charged groups and are used for the exchange of cations, while anion exchanges carry many positively charged groups and function for the exchange of anions.

Procedure: In most cases, ion exchangers are used in the form of countercurrent columns, employing apparatus that is essentially similar to that used in chromatographic separations. When cation exchange is desired, the resin is first charged with hydrogen ions by soaking it, in bead or coarse powder form, in 2N hydrochloric acid for a few hours. This, in addition, allows for the swelling of the resin before it is packed in the glass tube, thus preventing possible breakage. After it is uniformly packed in the tube, a further adequate volume of 2N hydrochloric acid is passed through the column making the effluent strongly acid at this stage. The column is then washed with water to remove the excess acid following which the solution for ion exchange is allowed to drain down the charged column of resin. As a result, the cations will be removed from the solution as they replace the hydrogen ions that were in association with the resin.

A similar procedure is followed with anion exchangers except that an alkali solution is used to charge the resin in place of the acid.

Exchange Capacity: The capacity of exchangers, anionic or cationic, is usually stated in milliequivalents of the ion per gram of dry exchanger. The resin must be adequately recharged when its exchange capacity is reached.

Applications: Ion exchange methods are extremely useful in many fields. Some examples where ion exchange has been effectively used are:

1. Deionization: Water can be deionized by the use of a series of cation and anion exchangers. The mixed bed method is employed, by combining a strong acid exchanger which removes cations and a strong base exchanger which removes anions. Calcium, magnesium, sulphate, chloride, carbonate and bicaronate ion are very effectively removed from water by this procedure.
2. Exchange of Ionic Constituents: Hard water can be softened if it is passed through a cation exchanger that has been charged with sodium ions. The magnesium and calcium ions in the hard water will replace the sodium ions in association with the resin, removing, as result, the cause of hardness in the water. Potassium salts of penicillin can be converted into the sodium salts in the same way. Similarly, streptomycin chloride is obtained from streptomycin sulphate by anion exchange.
3. Separation of Ionic Compounds: By the proper use of exchangers that take up only one or group of components from a mixture, the undesired constituents in a particular combination can be removed. Ionic materials can be eliminated from penicillin solutions by a series of anion and cation exchangers.
4. Recovery Processes: Very small quantities of desirable ionic substances in large volumes of solutions containing non-ionic waste material can be isolated by ion exchange. Aneurine can be very easily separated from yeast wastes by this process.
5. Quantitative Analysis: Estimation of many ionic substances in aqueous solution can be achieved by ion exchange methods.
6. Physico-chemical constants: Activity coefficients are but some of the various other physico-chemical constants that have been determined by the use of ion exchange.

L. N. ELOWE.

XU

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Jenkins, B.W.: GP 9(6):66

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